Radiosensitizing Effect of Gold Nanoparticles under kV- and MV- X-ray Irradiations

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Abstract

Introduction:
As a possible radiosensitizer in radiotherapy, we investigated the generation of reactive oxygen species (ROS) from dispersed gold nanoparticles (AuNPs) with average diameters of 5-60nm under clinical X-ray irradiation[1][2]. The same AuNPs were added to the cultures of HeLa cells and their survivability was measured. Contribution of ROS generation to the cell survivability was discussed.

Materials and Methods:
Concentrations of AuNPs (BBI solutions) were changed at 0, 36, 72, and 144μM in 96 multi-well plates. ROS generation was measured by a fluorescent reagent Aminophenyl fluorescein (APF, Sekisui Medical), which is sensitive to hydroxyl radicals (OH▪). The integrated X-ray doses were varied from 1 to 10.0 Gy. A Mitsubishi linac (Model:EXL-15SP) was operated at 10MV with a dose rate of 1Gy/min. Survivability of HeLa cells were measured by absorbance of WST-1 (Roche) at 440nm.

Results and discussion:
APF fluorescent intensity indicated that ROS generation for 20 – 80nm Au colloids was greater than that of distilled water by a factor of 5-7 in a concentration-dependent way (Fig.1). Because of APF's specific sensitivity, we consider that OH▪ was a major species generated under x-ray irradiation. Regardless of the same mass density, ROS generation in 5nm and 10nm colloids was suppressed. With the addition of 75μM 5-60nm AuNPs in HeLa cell cultures for 24hours, X-ray doses up to 10Gy were given. The cell survivability was decreased as the X-ray doses. Sensitizing effect was observed over the entire dose range for 5nm AuNPs, and over the low doses up to 5Gy for 20nm and 40nm AuNPs. Sensitizing effect was not observed for 60nm AuNPs over the entire dose range.

Conclusion:
AuNPs function as a possible x-ray sensitizer by causing damage with a augmented effect of OH▪. Particles size can be a key factor in ROS generation and cell damage.

References

[1] Misawa M, Takahashi J., **Nanomedicine** 7(5) (2011), 604-14.
[2] Takahashi J., Misawa M., **Radiation Physics and Chemistry** 78(11) (2009) 889-98.

Figures

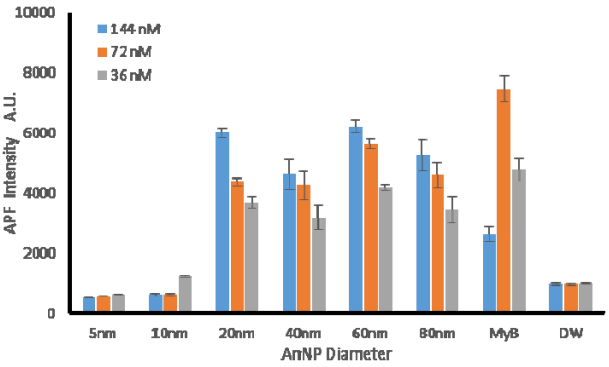

Fig.1 APF fluorescent intensity indicates ROS generation. Over 20nm AuNPs showed enhanced ROS generation relative to distilled water by a factor of 5-7.

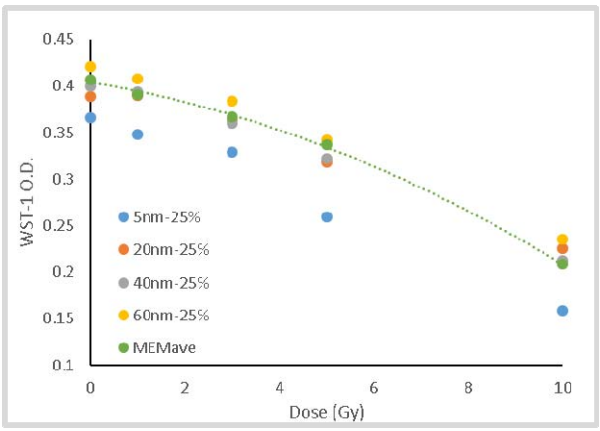

Fig.2 Decrease in HeLa cell survivability as the X-ray dose. 5-40nm AuNPs showed sensitization effect.